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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,522	02/11/2002	Cristian L. Achim	214001-00823-1	5288

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EXAMINER

NICHOLS, CHRISTOPHER J.

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/073,522

Applicant(s)

ACHIM ET AL.

Examiner

Christopher J Nichols, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 7-36 is/are pending in the application.
- 4a) Of the above claim(s) 3,7-13,16 and 18-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,14,15,17 and 29-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-4 and 7-36 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Advisory Action

1. **The finality of the previous Office Action (3 December 2003) is hereby withdrawn and prosecution on the merits reopened as the Amendment filed 8 March 2004 has overcome the previous rejections under 35 U.S.C. §112 ¶1.**

Status of Application

2. The Response and Amendment filed 8 March 2004 has been received and entered in full.
3. The rejection of claims **1, 2, 4-6, 14, 15, 17, and 29-36** under 35 U.S.C. §112 ¶1 as set forth at ¶7-11 pp. 3-4 in the previous Office Action (3 December 2003) is hereby *withdrawn* in view of Applicant's amendments (8 March 2004).
4. The rejection of claims **5 and 6** under 35 U.S.C. §112 ¶2 as set forth at ¶12-15 pp. 4-5 in the previous Office Action (3 December 2003) is *moot* in view of Applicant's cancellation of said claims (8 March 2004).
5. All rejections and objections not herein set forth or maintained are *withdrawn*.

Claim Objections

6. Claim **34** is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 34 is drawn to "stroke" wherein parent claim 1 is drawn to "ischemic cerebral stroke", a species of the larger genus "stroke" {see Stedman's Medical

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Dictionary 27th Edition (2000) Lippincott Williams & Wilkins}. Therefore the dependent claim 34 broadens the scope of what was presented in the parent claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims **1, 2, 14, 15, 29, and 31-36** rejected under 35 U.S.C. 102(e) as being anticipated by US 6,258,353 B1 (10 July 2001) Isacson *et al.*
8. US 6,258,353 teaches a method to treat neurodegenerative disorders in humans comprising transplanting porcine neural cells into patients thus meeting the limitations of claims 1 and 14 (Example VIII; claims 1-26).
9. US 6,258,353 teaches practicing its claimed method to treat disorders including but not limited to Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Alzheimer's disease, and cerebral stroke thus meeting the limitations of claims 1, 14, 32, 33, 34, 35, and 36 (Col 6 lines 6, 15-30).
10. US 6,258,353 teaches practicing its claimed method including the step of culturing the porcine neural cells with cyclosporin A (also known as cyclosporine A see Sigma Product Information included herein) or FK506 prior to transplantation thus meeting the limitations of claims 1, 14, 29, and 31 (Col 4 lines 60-65; Col. 5 lines 15-18; Col. 22 lines 20-50). Although

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cyclosporin A and FK506 are used to achieve a “desired therapeutic effect”, a compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)).

Therefore the cyclosporin A and FK506 used by US 6,258,353 will “promote growth, survival and integration” as these may be construed as desired therapeutic effects.

11. US 6,258,353 teaches practicing its claimed method including the step of administering cyclosporin A or FK506 to the subject (patient) thus meeting the limitations of claims 2 and 15 (Col 5 lines 29-43).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 4, 14, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,258,353 B1 (10 July 2001) Isacson *et al.* and White *et al.* (January-February 1999) “Neuron-Enriched Second Trimester Human Cultures: Growth Factor Response and In Vivo Graft Survival.” Cell Transplantation 8(1): 59-73 in view of Hale *et al.* (15 February 1997)

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“Superiority of sirolimus (rapamycin) over cyclosporine in augmenting allograft and xenograft survival in mice treated with antilymphocyte serum and donor-specific bone marrow.”

Transplantation 63(3): 359-64.

13. US 6,258,353 teaches a method to treat neurodegenerative disorders in humans comprising transplanting porcine neural cells into patients thus meeting the limitations of claims 1 and 14 (Example VIII; claims 1-26).

14. US 6,258,353 teaches practicing its claimed method to treat disorders including but not limited to Parkinson’s disease, Huntington’s disease, amyotrophic lateral sclerosis, Alzheimer’s disease, and cerebral stroke thus meeting the limitations of claims 1 and 14 (Col 6 lines 6, 15-30).

15. US 6,258,353 teaches practicing its claimed method including the step of culturing the porcine neural cells with cyclosporin A (also known as cyclosporine A see Sigma Product Information included herein) or FK506 prior to transplantation thus meeting the limitations of claims 1 and 14 (Col 4 lines 60-65; Col. 5 lines 15-18; Col. 22 lines 20-50). Although cyclosporin A and FK506 are used to achieve a “desired therapeutic effect”, a compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). Therefore the cyclosporin A and FK506 used by US 6,258,353 will “promote growth, survival and integration” as these may be construed as desired therapeutic effects.

16. US 6,258,353 teaches practicing its claimed method including the step of administering cyclosporin A or FK506 to the subject (patient) (Col 5 lines 29-43).

17. US 6,258,353 *does not* teach, however, the use of second trimester human fetal neuronal cells or rapamycin (the limitations of claims 4 and 17).

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18. White *et al.* (1999) teaches that second trimester human fetal brain cells are good candidates for cell transplantation therapy for Parkinson's disease, a form of neurodegenerative illness thus meeting the limitations of claims 1, 4, 14, and 17 (pp. 59 and 71).
19. Hale *et al.* (15 February 1997) "Superiority of sirolimus (rapamycin) over cyclosporine in augmenting allograft and xenograft survival in mice treated with antilymphocyte serum and donor-specific bone marrow." Transplantation 63(3): 359-64 teaches that rapamycin is a potent immunosuppressive agent with great therapeutic potential. Rapamycin was superior to cyclosporine in augmenting donor BM-induced skin graft prolongation in ALS-treated mice across all levels of histoincompatibility.
20. It would have been obvious to a person of ordinary skill in the art at the time of the invention was made to use second trimester human fetal brain cells of White *et al.* (1999), pre-treat them with rapamycin as taught by Hale *et al.* (15 February 1997) "Superiority of sirolimus (rapamycin) over cyclosporine in augmenting allograft and xenograft survival in mice treated with antilymphocyte serum and donor-specific bone marrow." Transplantation 63(3): 359-64 in the cell transplantation therapy as taught by US 6,258,353.
21. A person of ordinary skill in the art at the time the invention was made would have been motivated to use rapamycin pretreated second trimester human fetal cells in the method of US 6,258,353 because of the advantages taught by White *et al.* (1999) concerning second trimester human fetal cell (pp. 60; 67-69) such as ease of manipulation and better survival post-transplant and the therapeutic effects of rapamycin as shown by Hale *et al.* Further US 6,258,353 teaches that xenotransplants (cross species cell transplantation procedures) can result in the transmission

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of a pathogenic organism (Col. 4 lines 40-45; Col. 17 lines 22-54); use of human fetal cells would avoid this problem.

22. A person of ordinary skill in the art at the time the invention was made would have a reasonable expectation of success because White *et al.* (1999) practices cell transplantation in SCID mice thereby demonstrating its use (pp. 67-69) and Hale *et al.* who showed that rapamycin has the additional valued effect of being active even with histoincompatible transplants.

23. Thus the invention as a whole was *prima facie* obvious over the prior art.

Summary

24. No claims are allowed.

25. The Examiner notes that rapamycin is also known as sirolimus and RAPAMUNE {see ADIS R&D Profile (January 1999) "Sirolimus AY 22989, NSC 226080, NSC 606698, Rapamycin, RAPAMUNE" Drugs R&D 1(1): 100-107}

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Conclusion

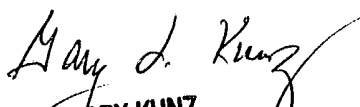
Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on **(571) 272-0887**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **<http://pair-direct.uspto.gov>**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

CJN

April 5, 2004


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